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Title: Glibenclamide mitigates cognitive impairment and hippocampal neuroinflammation in rats with type 2 diabetes and sporadic Alzheimer-like disease

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Source: BEHAVIOURAL BRAIN RESEARCH **Volume:** 379 **Article Number:** 112359 **DOI:** 10.1016/j.bbr.2019.112359 **Published:** FEB 3 2020

Times Cited in Web of Science Core Collection: 6

Total Times Cited: 6

Usage Count (Last 180 days): 1

Usage Count (Since 2013): 6

Cited Reference Count: 93

Abstract: A growing body of evidence suggests that type 2 diabetes (T2D) is a risk factor for cognitive impairment and dementia. Both preclinical and clinical studies have provided evidence that brain insulin resistance is associated with cognitive decline in patients with T2D and sporadic Alzheimer disease (AD). Accordingly, antidiabetic medications have been suggested as potential drugs for the treatment of cognitive impairments in patients with sporadic AD. This study set out to determine whether glibenclamide (GBC), an antidiabetic agent, can ameliorate cognitive impairments in rats with T2D and sporadic AD. Both animal models were treated with GBC for 23 consecutive days. To assess working and spatial memory, animals were subjected to the Y-maze and Morris water-maze tests. We measured glucose and insulin levels in the blood, and inflammatory cytokines such as tumor necrosis factor (TNF)-alpha and interleukin (IL)-6 in the hippocampus of animals. Our findings indicated that T2D and sporadic AD impaired memory and elevated TNF-alpha and IL-6 in the hippocampus. We found increased glucose and insulin levels in the blood of T2D-induced rats but not of sporadic AD rats. In contrast, GBC treatment improved memory impairment, increased insulin, and reduced glucose and hippocampal inflammation in rats with T2D and sporadic AD. This study suggests that GBC could be considered as a potential treatment for cognitive deficits in patients with T2D and sporadic AD. Taken together, this study highlights the need for further studies in humans to test whether GBC treatment is associated with cognitive improvement in sporadic AD patients.

Accession Number: WOS:000526062200049

PubMed ID: 31733313

Language: English

Document Type: Article

Author Keywords: Memory; Insulin resistance; Streptozotocin; Sulfonylurea; TNF-alpha; IL-6

KeyWords Plus: TUMOR-NECROSIS-FACTOR; BRAIN INSULIN-RESISTANCE; TNF-ALPHA; MOUSE MODEL; IMPROVES COGNITION; MEMORY DYSFUNCTION; FUSION PROTEIN; ANIMAL-MODEL; INTERLEUKIN-6; INFLAMMATION

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Publisher: ELSEVIER

Publisher Address: RADARWEG 29, 1043 NX AMSTERDAM, NETHERLANDS

Web of Science Categories: Behavioral Sciences; Neurosciences

Research Areas: Behavioral Sciences; Neurosciences & Neurology

IDS Number: LD5ID

ISSN: 0166-4328

eISSN: 1872-7549

29-char Source Abbrev.: BEHAV BRAIN RES

ISO Source Abbrev.: Behav. Brain Res.

Source Item Page Count: 9

Funding:

Funding Agency	Grant Number
Qazvin University of Medical Sciences	720

This study was supported by a grant from Qazvin University of Medical Sciences (No. 720).

Output Date: 2020-12-15

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